

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/27/2009 has been entered.

Claims 1-21 and 23-35 are currently pending. Claims 1, 4, 15 and 28 have been amended. Claim 22 has been canceled and no claims have been added.

Claims 23-35 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/05/2007.

Claims 1-21 have been examined on their merits.

### ***Previous Rejections***

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

***Response to Amendment***

The declaration filed on 08/27/2009 under 37 CFR 1.131 has been considered but is ineffective to overcome the Jensen et al reference.

The evidence submitted is insufficient to establish diligence from a date prior to the date of reduction to practice of the Jensen et al reference to either a constructive reduction to practice or an actual reduction to practice. The claims have been amended to include the limitation "wherein the maximum chamber volume is 1  $\mu$ L". Since the evidence provided by Applicant does not make any mention of chamber volume it is deemed to be insufficient to show diligence for the **current** claims prior to the date of the Jensen et al reference.

The evidence submitted is insufficient to establish a conception of the invention prior to the effective date of the Jensen et al reference. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897). Since the evidence provided by Applicant does not make any mention of chamber volume it is deemed to be insufficient to show diligence for the current claims prior to the date of the Jensen et al reference.

In addition, the missing signature of one of the inventors has not been properly addressed. According to MPEP 715.04, where one or more of the named inventors of the subject matter of the rejected claim(s) (who had originally signed the oath or

declaration for patent application under 37 CFR 1.63) is now unavailable to sign an affidavit or declaration under 37 CFR 1.131, the affidavit or declaration under 37 CFR 1.131 may be signed by the remaining joint inventors provided a petition under 37 CFR 1.183 requesting waiver of the signature of the unavailable inventor be submitted with the affidavit or declaration under 37 CFR 1.131. Proof that the non-signing inventor is unavailable or cannot be found similar to the proof required for a petition under 37 CFR 1.47 must be submitted with the petition under 37 CFR 1.183 (see MPEP § 409.03(d)). Petitions under 37 CFR 1.183 are decided by the Office of Petitions (see MPEP § 1002.02(b)).

Applicant has indicated that a search for the co-inventor Craig Gershater has been unsuccessful. However the Examiner's search of the internet has shown that a Craig Gershater (former CEO of Cambridge Bioprocess management) presented a workshop on March 16-18 2009 at the Advanced Centre for Biochemical Engineering at University College, London. It is suggested that perhaps this program might assist Applicant in locating Craig Gershater for any necessary signatures.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1-5, 7-11, 13-16, 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen et al (US 2004/0077075) in view of Tüdös et al (Lab on a Chip, 2001) and O'Connor et al (US 6,561,208).**

Amended claim 1 is drawn to a method for monitoring cells in a microfluidic device comprising: feeding the cells into the microfluidic device through one or more microfluidic channels, wherein the device includes a chamber comprising a sensor, and

wherein the maximum chamber volume is 1  $\mu$ L; and monitoring the cells under conditions such that attachment of the cells to the surface of the chamber is inhibited.

Dependent claims include wherein the chamber surface comprises a gas-permeable material (claim 2); wherein the gas is selected from a group (claim 3); wherein the material is a fluoropolymer (claim 4); wherein the chamber surface comprises a hydrophilic material (claim 5); wherein the chamber is formed in epoxy resin coated on a plastics substrate (claim 7); wherein the plastics substrate is polycarbonate (claim 8); wherein the chamber comprises a plurality of sensors (claim 9); wherein the sensor is sensitive to oxygen, carbon dioxide, ammonium or pH (claim 10); wherein the sensor is optical or electrochemical or acoustic (claims 11 and 13); wherein the sensor is sensitive to a reactant or product of fermentation (claim 14); wherein the volume of the chamber is from 50 nL to 1  $\mu$ L (claim 15); further comprising introducing growth medium into the chamber, wherein the sensor is sensitive to a reactant or product of cell growth (claim 16); further comprising introducing a component derived from the cells into a second microfluidic chamber comprising a sensor and in connection with the first chamber detecting the component (claim 19); wherein the component is a product of cell growth (claim 20); and wherein the component is an expressed protein or enzyme (claim 21).

Jensen et al teach a microfluidic device for use in monitoring and culturing cells. The microfluidic device is a vessel having an interior volume of less than 200 ml and in particular 5  $\mu$ L (page 4 para 61) and which has an aeration membrane made of a fluoropolymer or silicone that allows oxygen diffusion to the growing cells (page 8 para

94). The surface of the chamber is modified to inhibit attachment of cells (page 8 para 97-99) and at least one analytical sensor is integrated into the device (page 10 para 112). Wherein the chamber surface comprises a hydrophilic material is taught (page 8 para 98-99) as well as wherein the chamber comprises a plurality of sensors, including optical and electrochemical (page 11 para 116) that are sensitive to oxygen, carbon dioxide or pH (page 11 para 117-127). The chamber is formed in an epoxy resin coated on a plastics substrate (page 18 para 206) and the substrate material includes polycarbonate (page 4 para 62). The analytical sensor detects or measures (is sensitive to) any cell metabolite or cell product such as a protein or enzyme (page 10 para 112). Introducing growth medium into the chamber, wherein the sensor is sensitive to a product of cell growth, is taught (page 1 para 7) as well as introducing a component derived from the cells into a second microfluidic chamber comprising a sensor and connected by a membrane with the first chamber detecting the component (page 1 para 10).

Jensen et al do not specifically teach wherein the maximum chamber volume is 1  $\mu\text{L}$ .

Tüdös et al teach that it is advantageous to perform bioassays on a microchip with a several thousand fold reduced sample volume down to less than 1  $\mu\text{L}$  (page 92, column 1). O'Connor et al teach that microfluidic devices with chambers with a maximum volume of 1  $\mu\text{L}$  are known in the art as well (column 14 lines 5-16).

Therefore one of ordinary skill in the art would have been motivated to use chamber volumes of 1  $\mu$ L or less in the method of Jensen et al because Tüdös et al and O'Connor et al teach that microfluidic chambers with volumes less than 1  $\mu$ L are known to be useful. One of ordinary skill in the art would have been motivated by the benefit of conserving space and resources as well. One of ordinary skill in the art would have had a reasonable expectation of success because Jensen et al teaches that smaller chambers are advantageous and can be less than 5  $\mu$ L in volume (page 4 para 61) and because O'Connor et al was also using microfluidic chambers less than 1  $\mu$ L in volume as well.

Therefore the combined teachings of Jensen et al, Tüdös et al and O'Connor et al render obvious Applicant's invention as claimed.

**Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen et al (US 2004/0077075) in view of Tüdös et al (Lab on a Chip, 2001) and O'Connor et al (US 6,561,208) as applied to claims 1-5, 7-11, 13-16, 19-21 above, and further in view of Wada et al (WO 99/67639-from IDS).**

Claim 6 is drawn to the method of claim 5 and includes wherein the hydrophilic material is polyvinyl alcohol.

Jensen et al teach the method of using the microfluidic device as described above and indicate that a number of different approaches may be employed to alter the

adsorptive properties of the contacting surfaces of the device and provide a hydrophilic surface (page 8 para 98-99).

Jensen et al do not specifically teach the use of polyvinyl alcohol as a hydrophilic material.

Wada et al teach a method for monitoring cells with a microfluidic device. The prevention of attachment of the cells to the interior surface of the device is taught as desirable and accomplished in a variety of ways such as using PVA (polyvinyl alcohol) coatings (page 25 line 31-page 26 line 7).

Therefore, one of ordinary skill in the art would have been motivated to use PVA as a coating on the surface of the microfluidic device of Jensen et al because Wada et al teach that a PVA coating is a suitable treatment to prevent cell attachment in a microfluidic device and Jensen et al teach the desire to prevent cell attachment as well. One of ordinary skill in the art would have had a reasonable expectation of success because both Jensen et al (page 8 para 95) and Wada et al (page 24 line 18) are using microfluidic devices of the same material (PDMS).

Therefore, the combined teachings of Jensen et al, Tüdös et al, O'Connor et al, and Wada et al render obvious Applicant's invention as claimed.

**Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen et al (US 2004/0077075) in view of Tüdös et al (Lab on a Chip, 2001) and**



**O'Connor et al (US 6,561,208) as applied to claims 1-5, 7-11, 13-16, 19-22 above, and further in view of Lowe et al (US 5,989,923).**

Claim 12 is drawn to the method of claim 11, wherein the sensor is a holographic sensor.

Jensen et al teach the method of using the microfluidic device as described above and indicate that there is a need to integrate available sensor technology (page 3 para 49).

Jensen et al do not specifically teach the use of holographic sensors with the microfluidic device.

Lowe et al teach a holographic sensor for measuring analytes (column 11 lines 18-46). In particular the sensor has applications in detecting biologically secreted proteins or proteases and is capable of detecting bacteria.

Therefore, one of ordinary skill in the art would have been motivated to apply the holographic sensors of Lowe et al to the microfluidic device of Jensen et al because Jensen et al indicate that more than one type of optical sensor may be used in the device to monitor cells (such as bacteria) and because Lowe et al teach that holographic sensors are suitable for optically interrogating bacteria. One of ordinary skill in the art would have had a reasonable expectation of success because Lowe et al teach that it is readily apparent that a holographic sensor may be fabricated whose characteristics are predictable (column 11 lines 22-25).

Therefore, the combined teachings of Jensen et al, Tüdös et al, O'Connor et al, and Lowe et al render obvious Applicant's invention as claimed.

**Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen et al (US 2004/0077075) in view of Tüdös et al (Lab on a Chip, 2001) and O'Connor et al (US 6,561,208) as applied to claims 1-5, 7-11, 13-16, 19-22 above, and further in view of Walker et al (US 5,474,774) and Qian et al (Analytical Chemistry 2002).**

Claim 17 includes wherein the growth medium comprises a non-metabolisable mannose analogue.

Claim 18 includes wherein the analogue is methyl  $\alpha$ -D-mannopyranoside.

Jensen et al teach the method of using the microfluidic device as described above and indicate that different approaches may be employed in inhibiting the attachment of the cells (pages 9-10, para 107).

Jensen et al do not specifically teach the addition of a non-metabolisable analogue of mannose, such as methyl  $\alpha$ -D-mannopyranoside.

Walker et al teach a method of inhibiting the adhesion of bacteria to devices, such as fermentation equipment, by applying an extract to a suitable medium to a surface having bacteria to disengage the bacteria from the surface (column 2 lines 32-49).

Qian et al teach that methyl  $\alpha$ -D-mannopyranoside is a compound that inhibits the adhesion of bacteria to surfaces (page 1808, column 2).

Therefore, one of ordinary skill in the art would have been motivated to use the non-metabolisable analogue of methyl  $\alpha$ -D-mannopyranoside as a compound to prevent bacterial adhesion in the device of Jensen et al because Walker et al teach that it is known in the art to add compounds that inhibit bacterial adhesion to a surface, such as a fermentation device, in a suitable medium and Qian et al teach that methyl  $\alpha$ -D-mannopyranoside is capable of inhibiting bacterial adhesion. One of ordinary skill in the art would have had a reasonable expectation of success because Jensen et al indicate that different approaches may be employed in inhibiting the attachment of the cells (pages 9-10, para 107).

Therefore, the combined teachings of Jensen et al., Tüdös et al, O'Connor et al, Walker et al and Qian et al render obvious Applicant's invention as claimed.

**Claims 1-4, 7-11, 13-16, 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freeman (US 6,653,124) in view of Tüdös et al (Lab on a Chip, 2001) and O'Connor et al (US 6,561,208).**

Freeman discloses a microscale bioreactor comprising a first vessel (Figure 3:12) having an interior volume of 1 ml or less for culturing cells. A second vessel (Figure 3:44) is separated from the first vessel at least in part by a membrane (Figure 3:40) permeable to oxygen and carbon dioxide and impermeable to cells. The semi permeable membrane allows diffusion of oxygen and carbon dioxide, but restricts the

passage of liquid and solid products. Membranes are selectively chosen to prevent or permit the movement of certain micromolecules. The membranes may be impermeable to cells, but be chosen to be permeable to nutrients and cell products. Inlet and outlet ports connected to channels for the addition and removal of liquids and gases are disclosed throughout the reference, and may inherently be in fluid communication with the second chamber. This is described in column 23, line 61 to column 26, line 3, and especially in column 24, line 49 to column 25, line 13. Cellular attachment to the substrate of the bioreactor may be discouraged as well (column 25 lines 15-20). Use of epoxy resin to coat the plastic substrates is also taught as desirable (column 16 lines 44-58). A plurality of sensors (column 30 lines 20-25) is also taught as well as the use of polycarbonate as the substrate (column 26 line 41). Optical as well as electrochemical sensing is suggested (column 29 lines 20-22) as well as the monitoring of cell growth and expressed proteins (column 1 lines 53-62). The use of fluoropolymers (such as Teflon) is also suggested as suitable (column 24 lines 22-23). Systems capable of regulating volumes as small as 10-1000 nanoliters are taught to be desirable (column 1 lines 29-31) and included (column 8 lines 60-62). Freeman suggests that the system is not limited to the specific embodiments and may be modified (column 29 lines 51-61) and therefore it would be obvious to combine the various options as Freeman suggests their suitability in a microfluidic system for the monitoring of cells.

Freeman does not specifically teach wherein the maximum chamber volume is 1  $\mu\text{L}$ .

Tüdös et al teach that it is advantageous to perform bioassays on a microchip with a several thousand fold reduced sample volume down to less than 1  $\mu\text{L}$  (page 92, column 1). O'Connor et al teach that microfluidic devices with chambers with a maximum volume of 1  $\mu\text{L}$  are known in the art as well (column 14 lines 5-16).

Therefore one of ordinary skill in the art would have been motivated to use chamber volumes of 1  $\mu\text{L}$  or less in the method of Freeman because Tüdös et al and O'Connor et al teach that microfluidic chambers with volumes less than 1  $\mu\text{L}$  are known to be useful. One of ordinary skill in the art would have been motivated by the benefit of conserving space and resources as well. One of ordinary skill in the art would have had a reasonable expectation of success because Freeman teaches that smaller chambers are advantageous and can be less than 20-400 nanoliters in volume (column 8 lines 60-62) and because O'Connor et al was also using microfluidic chambers less than 1  $\mu\text{L}$  in volume as well.

Therefore the combined teachings of Freeman, Tüdös et al and O'Connor et al render obvious Applicant's invention as claimed.

**Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freeman (US 6,653,124) in view of Tüdös et al (Lab on a Chip, 2001) and O'Connor et al (US 6,561,208) as applied to claims 1-4, 7-11, 13-16, 19-21 above, and further in view of Wada et al (WO 99/67639-from IDS).**

Claim 6 is drawn to the method of claim 5 and includes wherein the gas permeable material of the chamber is a hydrophilic material such as polyvinyl alcohol.

Freeman teaches the method of using the microfluidic device as described above and indicate that a number of different microfluidic substrate materials may be used to provide various surface materials (column 13 line 54- column 14 line 32, column 24 lines 12-23).

Freeman does not specifically teach the use of polyvinyl alcohol as a hydrophilic material for the gas permeable material of the chamber surface.

Wada et al teach a method for monitoring cells with a microfluidic device. The prevention of attachment of the cells to the interior surface of the device is taught as desirable and accomplished in a variety of ways such as using PVA (polyvinylalcohol) coatings (page 25 line 31-page 26 line 7).

Therefore, one of ordinary skill in the art would have been motivated to use PVA as a coating on the surface of the microfluidic device of Freeman because Wada et al teach that a PVA coating is a suitable treatment to prevent cell attachment in a microfluidic device and Freeman teaches the desire to prevent cell attachment as well (column 25 lines 15-20). One of ordinary skill in the art would have had a reasonable expectation of success because both Freeman (column 26 lines 35-41) and Wada et al (page 24 line 18) are using microfluidic devices of the same material (PDMS).

Therefore, the combined teachings of Freeman, Tüdös et al, O'Connor et al, and Wada et al render obvious Applicant's invention as claimed.

**Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Freeman (US 6,653,124) in view of Tüdös et al (Lab on a Chip, 2001) and O'Connor et al (US 6,561,208) as applied to claims 1-4, 7-11, 13-16, 19-22 above, and further in view of Lowe et al (US 5,989,923).**

Claim 12 is drawn to the method of claim 11, wherein the sensor is a holographic sensor.

Freeman teaches the method of using the microfluidic device as described above and indicates that there is a need to integrate available sensor technology (column 29 lines 45-50).

Freeman does not specifically teach the use of holographic sensors with the microfluidic device.

Lowe et al teach a holographic sensor for measuring analytes (column 11 lines 18-46). In particular the sensor has applications in detecting biologically secreted proteins or proteases and is capable of detecting bacteria.

Therefore, one of ordinary skill in the art would have been motivated to apply the holographic sensors of Lowe et al to the microfluidic device of Freeman because Freeman indicates that more than one type of optical sensor may be used in the device to monitor cells and microorganisms (such as bacteria) (column 1 lines 55-62) and because Lowe et al teach that holographic sensors are suitable for optically interrogating bacteria. One of ordinary skill in the art would have had a reasonable expectation of success because Lowe et al teach that it is readily apparent that a

holographic sensor may be fabricated whose characteristics are predictable (column 11 lines 22-25).

Therefore, the combined teachings of Freeman, Tüdös et al, O'Connor et al, and Lowe et al render obvious Applicant's invention as claimed.

**Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freeman (US 6,653,124) in view of Tüdös et al (Lab on a Chip, 2001) and O'Connor et al (US 6,561,208) as applied to claims 1-4, 7-11, 13-16, 19-22 above, and further in view of Walker et al (US 5,474,774) and Qian et al (Analytical Chemistry 2002).**

Claim 17 includes wherein the growth medium comprises a non-metabolisable mannose analogue.

Claim 18 includes wherein the analogue is methyl  $\alpha$ -D-mannopyranoside.

Freeman teaches the method of using the microfluidic device as described above and indicates that different approaches may be employed in inhibiting the attachment of the cells (column 25 lines 15-20).

Freeman does not specifically teach the addition of a non-metabolisable analogue of mannose, such as methyl  $\alpha$ -D-mannopyranoside.

Walker et al teach a method of inhibiting the adhesion of bacteria to devices, such as fermentation equipment, by applying an extract to a suitable medium to a



surface having bacteria to disengage the bacteria from the surface (column 2 lines 32-49).

Qian et al teach that methyl  $\alpha$ -D-mannopyranoside is a compound that inhibits the adhesion of bacteria to surfaces (page 1808, column 2).

Therefore, one of ordinary skill in the art would have been motivated to use the non-metabolisable analogue of methyl  $\alpha$ -D-mannopyranoside as a compound to prevent bacterial adhesion in the device of Freeman because Walker et al teach that it is known in the art to add compounds that inhibit bacterial adhesion to a surface, such as a fermentation device, in a suitable medium and Qian et al teach that methyl  $\alpha$ -D-mannopyranoside is capable of inhibiting bacterial adhesion. One of ordinary skill in the art would have had a reasonable expectation of success because Freeman indicates that different approaches may be employed in inhibiting the attachment of the cells (column 25 lines 15-20).

Therefore, the combined teachings of Freeman, Tüddös et al, O'Connor et al, Walker et al and Qian et al render obvious Applicant's invention as claimed.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**Claims 1, 3, 9-12, 14, 16, 19, 20, remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 8 of copending Application No. 10/520,221 in view of Tüdös et al (Lab on a Chip, 2001) and O'Connor et al (US 6,561,208).**

Although the conflicting claims are not identical, they are not patentably distinct from each other because they disclose inventions with the same limitations. It is noted that instant claim 1 requires that the cell is inhibited from attachment to the surface of the chamber, whereas claim 1 of copending 10/520221 requires that the cell be immobilized. However these limitations do not exclude wherein a cell is immobilized on a bead that is then inhibited from attachment to the surface of the chamber. Therefore the claims, as recited, are overlapping. The use of chambers with a maximum volume of 1  $\mu$ L is also deemed to be an obvious modification based on the teachings of Tüdös et al and O'Connor et al.

Tüdös et al teach that it is advantageous to perform bioassays on a microchip with a several thousand fold reduced sample volume down to less than 1  $\mu$ L (page 92, column 1). O'Connor et al teach that microfluidic devices with chambers with a maximum volume of 1  $\mu$ L are known in the art as well (column 14 lines 5-16).

Therefore one of ordinary skill in the art would have been motivated to use chamber volumes of 1  $\mu$ L or less in the method of the copending application because Tüdös et al and O'Connor et al teach that microfluidic chambers with volumes less than 1  $\mu$ L are known to be useful. One of ordinary skill in the art would have been motivated by the benefit of conserving space and resources as well. One of ordinary skill in the art would have had a reasonable expectation of success because O'Connor et al was using microfluidic chambers less than 1  $\mu$ L in volume as well.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura Schubert whose telephone number is (571)272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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